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Impact of a pharmacy benefit change on new use of mail order pharmacy among diabetes patients: The Diabetes Study of Northern California (DISTANCE)

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Abstract

Objective—To assess the impact of a pharmacy benefit change on mail order pharmacy (MOP) uptake.

Data sources/study setting—Race-stratified, random sample of diabetes patients in an integrated healthcare delivery system.

Study Design—In this natural experiment, we studied the impact of a pharmacy benefit change that conditionally discounted medications if patients used MOP and prepaid 2 copayments. We compared MOP uptake among those exposed to the benefit change (n=2,442) and the reference group with no benefit change (n=8,148), and estimated differential MOP uptake across social strata using a difference-in-differences framework.

Data collection/extraction methods—Ascertained MOP uptake (initiation among previous non-users).

Principal findings—Thirty percent of patients started using MOP after receiving the benefit change vs. 9% uptake among the reference group ($p<0.0001$). After adjustment, there was a 26 percentage point greater MOP uptake (benefit change effect). This benefit change effect was significantly smaller among patients with inadequate health literacy (15% less), limited English proficiency (14% less) and among Latinos and Asians (24% and 15% less compared to Caucasians).

Conclusions—Conditionally discounting medications delivered by MOP effectively stimulated MOP uptake overall while unintentionally widened previously existing social gaps in MOP use because it stimulated less MOP uptake in vulnerable populations.

Keywords

mail order pharmacy; pharmacy benefit designs; comparative effectiveness; health disparities; difference-in-differences; marginal structural model; inverse probability treatment weighting

INTRODUCTION

Mail order pharmacies (MOP) dispense medications by mail to the patient's home, offering convenience and eliminating access barriers (e.g., time, mobility, transportation), the

benefits of which may be compounded for patients using multiple medications.(Choudhry et al. 2011) Currently, one-third of all chronic disease prescriptions in the United States are dispensed by mail.(2005) We have previously demonstrated better adherence (Duru et al. 2010), better LDL-C control(Schmittdiel et al. 2011), and no substantive safety concerns(Schmittdiel et al. 2013) among diabetic patients using MOP. Better adherence among those using MOP has been reported in other studies as well.(Devine, Vlahiotis, and Sundar 2010; Visaria 2012; Zhang et al. 2011)

Compared to walk-in pharmacies, MOP can also be cost-saving for the health plan, depending on differential wastage rates between the two delivery modes, the cost of increased drug utilization, and the size of any MOP incentives.(Carroll 2006; Carroll et al. 2005; Devine et al. 2010; Valluri et al. 2007) The World Health Organization recommends seeking effective and low-cost, structural (system-level) approaches to improving adherence as an alternative to the frequently expensive, individual-level interventions.(Sabate 2003) Financial incentives for MOP may represent such a system-level approach if they increase the use of MOP and secondarily improve adherence and health outcomes.

However, structural changes can simultaneously improve population-level quality metrics, while also increasing social inequalities in health access and outcomes. We have previously reported lower use of MOP among minorities and those living in deprived neighborhoods. (Duru et al. 2010) While MOP use has been increasing steadily over the past two decades, (Carroll et al. 2005) underuse in vulnerable groups has been observed at Kaiser Permanente Northern California (KPNC) since MOP was introduced in 1999 (unpublished data). For example, in 2000, the prevalence of MOP use was 11% in Latinos, 12% in African Americans and Filipinos, 20% in Asians and 24% in Caucasians. A decade later, in 2010, MOP use grew considerably, but still lagged substantially in minorities: 37% in Latinos and African Americans, 46% in Filipinos, 63% in Asians and 65% in Caucasians. It is unknown whether and how financial incentives might impact disparities in MOP use.(Trinacty et al. 2009)

We studied a natural experiment which included a pharmacy benefit change that increased cost-sharing, but promoted the use of MOP by discounting medications (i.e., reducing the increase in out-of-pocket costs) if patients prepaid 2 copayments and refilled using MOP. We evaluated: 1) the overall effect of rolling out the benefit change on subsequent uptake of MOP for dispensing of cardiometabolic medications among patients with diabetes, and 2) whether the rollout's effect on MOP uptake was uniform across social strata (defined by ethnicity, educational attainment, household income, English proficiency or health literacy).

METHODS

Setting

This study was conducted in KPNC, an integrated, health care delivery system that provides medical care to ~3 million members (~30% of the population of the catchment, with ethnic and socioeconomic distributions similar to the general population, although fewer very poor or rich members).(Gordon and Kaplan 1991)

KPNC health plan pharmacy benefits are available only through KPNC's ~120 community pharmacies or, since 1999, via MOP. Although most new prescriptions are first dispensed at community pharmacies,(Valluri et al. 2007) KPNC patients may also fill new prescriptions by mail, with telephone access to a pharmacist who can answer medication-related questions after completing a simple enrollment process (by mail, phone or website). Unlike some MOP systems, KPNC patients must request (by mail, phone or website) each MOP dispensing and provide payment in advance (by credit card or check) before the medication is mailed (no automatic refills). Medications usually arrive within one week.

Intervention

Prior to January 1, 2006, the standard KPNC drug plan for all subjects required one copayment per dispensing (regardless of days' supply or mode of delivery). Effective January 1, 2006, all individual Medicare Senior Advantage members and select commercial and employer groups were changed to a new, less generous drug benefit package (more cost-sharing), which also included an incentive, in the form of a prepayment discount, to use MOP. The change in drug benefit was not a matter of individual choice, but rather based on employer group contracts. Impacted health plan members, which typically included more socially vulnerable subjects, were mailed an announcement describing the benefit changes and the MOP discount; originally in English only, translated versions of the announcement were available in the following year. The new benefit provided a 1, 2 or 3 months' supply at community pharmacies at a charge of 1, 2, or 3 copayments, respectively. Alternatively, patients could use MOP and receive a one months' supply for 1 copayment or use the prepaid discount which incentivized use of MOP by receiving 3-months' supply for 2 copayments (Figure 1). Thus a patient who was willing and able to prepay two copayments would receive a 100-day supply from the MOP compared with a 60-day supply from the walk-in pharmacy (i.e., 40 extra days' supply for using MOP).

To illustrate, consider a scenario among patients whose benefits contract had stipulated a $10 copayment per dispensing (typically, a 3-month supply); that is, prior to the 01/01/2006 benefit change, all patients would have been charged $10 for each dispensing of a standard 3 month supply, regardless of whether they used a walk-in pharmacy or mail order pharmacy. Among those patients who had no change in benefits, that copayment remained unaltered after 01/01/2006. In contrast, patients who had a benefit change would now pay $10 for each one-month supply; however, they could get a better deal if they used the MOP and requested three one-month supplies. That is, patients with the benefit change who obtained their medications via walk-in pharmacy would pay $10 for each one-month supply. However, if they chose to use mail order pharmacy, they would pay $10 for each one month supply, or $20 for a three month supply. Thus, the mail order prepayment discount permitted them to pay one copayment less ($10 in this scenario) for a 3 month supply compared to using a walk-in pharmacy. Thus their cost share for a 3 month supply changed from $10 (before the change) to $30 for medications obtained via walk-in pharmacy or $20 for medications obtained via mail order pharmacy. Therefore, the prepayment discount to use MOP did not offset the increase in cost sharing for those switched to the new, less generous benefit.

Participants

Study subjects were drawn from a cohort of 20,188 adults who were respondents (62% response rate) in the *Diabetes Study of Northern California (DISTANCE)* Survey, an ethnically stratified, random sample of diabetes members identified prior to January 1, 2005, (Moffet et al. 2008) The DISTANCE survey was offered in English, Spanish, Mandarin, Cantonese or Tagalog, and included a wide range of social factors that we hypothesized to be associated with social disparities in health care use and outcomes. To study the effect of the pharmacy benefit change among non-users of MOP, we limited the study population to diabetes patients not offered incentives to use MOP nor using MOP prior to baseline, and dispensed at least one of the cardiometabolic medication used as primary treatment for diabetes patients (anti-glycemic, anti-hypertensive or lipid-lowering). Thus, we excluded the 5,216 subjects who used MOP during the 12 months prior to baseline (January 1, 2006); we also excluded 1,131 subjects not dispensed any cardiometabolic medication during the two years prior to baseline (January 1, 2004 – December 31, 2005) or during the year after baseline (January 1, 2006 – December 31, 2006), and 3,251 who either lacked continuous Kaiser membership or a standard pharmacy benefit contract throughout the observation window. This yielded an analytic sample of 10,590 subjects, of which 2,442 (23%) had a benefit change and 8,148 (77%) had no change, serving as the reference group.

Outcomes and follow-up

Initiation of MOP use (“uptake”) was defined as having at least one MOP dispensing for a cardiometabolic medication in the 12 months after baseline (among previous non-users). Our goal was to estimate the effect of the pharmacy benefit change on MOP uptake overall and across social groups defined by self-reported ethnicity, educational attainment, annual income, self-reported financial hardship (self-reported difficulties purchasing needed medications(Chien-Wen et al. 2002), medical supplies or food (Ross and Wu 1995) due to insufficient funds), limited English proficiency (always or often having problems speaking or reading English), and a validated measure of health literacy (problems understanding health education materials or instructions(Chew, Bradley, and Boyko 2004)).

Statistical Analysis

We used a difference-in-differences (DID) framework to study the impact of the benefit change on mail order uptake (“benefit change effect”). This benefit change effect was then contrasted (again using DID) across social groups by estimating the adjusted, absolute difference between the benefit change effect for any given social group and the reference social category (e.g., benefit change effects for African American minus benefit change effects for Caucasian); this estimate was called the “effect difference”. DID is a quasi-experimental approach used to study change in an outcome before and after an intervention, after “netting out” the background change in rates due to effect of secular time trends and aging on that same outcome identified in a reference group who was not affected by the intervention.(Campbell and Stanley 1963; Meyer 1995) Regression to the mean is not a concern given both exposed and reference group have the identical starting point (none are MOP users at baseline). In the context of this study, the benefit change effect on mail order uptake was estimated by the uptake during the year following the benefit change after

subtracting the background secular time trends estimated by MOP uptake in those not experiencing the benefit change (reference group).

DID rests on the assumption that the unobservable (i.e., counterfactual) outcome in the exposed group, if they hadn't been exposed to the intervention, would be qualitatively similar to the observable outcome in the unexposed reference group. That is, if the group exposed to the changes in the benefits, had (counterfactually) not been exposed to those benefit changes, then we assume their MOP uptake would be similar to that observed in the reference group. We examined the validity of the DID assumption by evaluating the MOP uptake in 2005 (the year prior to the exposure) among subjects who had no MOP use as of 01/01/2005, selecting the "soon-to-be-exposed" subjects who would receive the benefit change in 01/01/2006 and comparing them to the remaining subjects (i.e., no benefit change in 2006) who made up the reference group. The 2005 rates of uptake of MOP in these two groups prior to the implementation of the new benefit design were similar, although not identical. There was a modestly larger MOP uptake among those who would later receive a change in benefits vs. the reference group (1.38 vs. 1.04 percentage points per month, respectively). Although the 2005 population used for this test of assumptions was not identical to the population used for the final analysis (since we excluded those who started using MOP during 2005 prior to the 01/01/2006 baseline), the qualitatively similar uptake suggest that the DID assumption should be reasonable. While selection into groups receiving the different benefit packages could introduce bias the estimate of the benefit effect, this bias is assumed uniform across social groups and thus hould not impact the estimate of benefit effect differences across social groups in a substantive way. However, while we present the quantitative DID results below, we will interpret those findings strictly as qualitative given this is an evaluation of a natural experiment that rests on unobservable assumptions.

We addressed potential confounding from measured and unmeasured risk factors by using each treated group as its own control, comparing potentially confounding risk factors before versus after the benefit change use during our study, and by controlling for demographic and clinical differences between those with the benefit change versus the reference group. Those prevalent differences were accounted for using a marginal structural modeling (MSM) approach based on the counterfactual theory of causality.(Mortimer et al. 2005; Robins 1999) The adjusted MSM models were weighted using a propensity score method called inverse probability of treatment weights (IPTW). The IPTW were derived from a pooled logistic regression model (R^2=77%): benefit change (yes/no) was regressed on baseline age, pharmacy copay for generic and brand medications, Medicare indicator, pharmacy benefit deductible indicator, pharmacy benefit business line (e.g., large employer group, small employer group, strategic group), ethnicity, income, education, limited English proficiency, inadequate health literacy or financial hardship). This weighting aligns the distribution in the comparison cohort of the variables used in the benefit change-probability model to match the distribution in the exposed group who experienced the benefits change. These estimates are unconfounded by the above adjustment variables under the assumption that the model is specified correctly. Models were further weighted to account for survey non-response (Horvitz and Source 1952) and the non-proportional sampling fractions (complex survey design). We estimated the adjusted, absolute benefit change effect (difference-in-differences) by specifying modified Poisson regression(Zou 2004) with robust standard

errors and an identity link function.(Cheung 2007) Confidence intervals were estimated using bootstrapping. We also conducted sensitivity analysis after excluding the 6% (n=991) of patients whose expenditures exceeded that covered by Medicare Part D (i.e., those reaching the coverage limit or "doughnut hole") during follow-up because financial incentives to use MOP would no longer be relevant while in the gap.

RESULTS

Subject Characteristics

The mean age of the subjects was 60 years, 50% were women, 80% minorities, 12% had limited English proficiency and 46% had inadequate health literacy (Table 1). Twenty-one percent had annual income <$25,000 and 38% self-reported difficulties paying for medications. Compared to the reference group, subjects who had a pharmacy benefit change had lower educational attainment, lower income, greater financial hardships, and more likely to have limited English proficiency, inadequate health literacy, and higher out of pocket costs for their cardiometabolic medications in the year prior to baseline. Prior to baseline, the average daily cost for medications in the benefit change versus reference groups was $0.23 versus $0.15, and the average out of pocket cost per dispensing was $13.65 versus $8.42, respectively. Thus, relative to patients in the reference group, those with the benefit change were already incurring more cost-sharing prior to the change. The majority of subjects were dispensed 3 month supplies at each fill before and after the roll-out of the benefit change. As expected with the introduction of a less generous cost sharing arrangement, the proportion dispensed 3 month supply at each fill dropped slightly (from 85.5% before the benefit change to 83.1% after the benefit change) among those exposed to the benefit change. For the reference group, the proportion went up slightly during the pre- vs. post-period (from 88.4% to 90.7%).

MOP uptake and Benefit Change Effect

Among those who did not previously use MOP, 30% of diabetes patients with the pharmacy benefit change initiated use of MOP in the year after the benefit change, as compared to 9% of patients not receiving the benefit change (Table 2). The benefit change effect was quantified by the absolute difference in uptake between the benefit change and reference groups, which was a difference of 21 percentage points (95% CI: 19%-23%) in the crude model and 26 percentage points (CI: 22%-30%) in the adjusted model.

Vulnerable social groups had a substantially smaller MOP uptake overall and were less responsive to the discount. Among those with the benefit change, the benefit change effect was higher among those with adequate health literacy (35% percentage point greater uptake (95% CI: 27% - 42%) compared to those with inadequate health literacy (20% percentage point greater uptake (CI: 14%-26%), representing 15 percentage points (CI: 5%, 24%) effect difference. Similarly, the benefit change effect was 27% percentage point greater uptake (CI: 23%-32%) among English-speaking patients, while among those with limited English proficiency only 13% (CI: 6%-21%), representing a 14% (CI: 5%, 22%) point effect difference. There were also significant race-ethnic effect differences relative to Caucasians; Latinos and Asians had a 24% [CI: 14%-33%)] and 16% [(CI: 0.1%-30%)] smaller benefit

change effect. A smaller benefit change effect was also observed among those with lower annual income, self-reported financial hardship, and fewer years of education, albeit not statistically significant after adjustment. There were no substantive differences in our findings when re-running the above analyses after excluding the 991 members who lost Part D Medicare pharmacy coverage during the observation window, and in separate models for Medicare and non-Medicare subjects.

Sensitivity Analysis

To disentangle the effect of the financial incentive for MOP from a patient's choice of length of supply, we conducted a sub-analysis in the 8,860 patients who would benefit from the incentive because they consistently filled 3 month supply in the periods before and after the benefit change. The adjusted MOP uptake was 28 percentage points greater in those who received the benefit change compared to those with no change in benefit (33% vs. 9% uptake) ($p<0.0001$). Thus, restricting to people who could benefit from the incentive because they always filled a 3 month supply yielded essentially the same answer as the main analysis (which estimated a 26% increase in MOP uptake). We then repeated that sensitivity analysis in the 741 patients who would not benefit from the incentive because they consistently filled less than 3 month supply during pre- and post periods and detected no significant difference in uptake among those who did vs. did not receive the benefit change.

DISCUSSION

We examined MOP uptake after a pharmacy benefit change which included a prepayment discount for use of MOP, while offering a less generous (more cost-sharing) pharmacy benefit package. We observed a substantial stimulating effect on MOP uptake. In the year following the benefit change, the MOP uptake among previous MOP non-users offered the prepayment discount to use MOP was a 26% points greater compared to those not offered the discount. Given existing disparities in MOP use and the potential for MOP to improve convenience, medication adherence and risk factor control, it is important to understand the effects of benefit changes and incentives on vulnerable populations. In general, patients behaved as price-sensitive consumers and the discount greatly stimulated MOP uptake population-wide. However, the effect of the benefit change on MOP was substantially smaller among minorities, those with inadequate health literacy or limited English proficiency.

Since the introduction of MOP at KPNC in 1999, minorities have consistently lagged behind Caucasians in the uptake of MOP and the reduced minority response to the MOP discount perpetuated the disparities. Similar patterns were observed in a recent study reporting that minorities or patients with inadequate health literacy or lower educational attainment were less likely to initiate use of a widely offered internet-based patient portal even if they had access to a computer.(Sarkar et al. 2010, 2011) The disparities in MOP use may have downstream impacts on disparities in medication adherence and clinical outcomes. We have previously reported better adherence(Duru et al. 2010) and better LDL-C control(Schmittdiel et al. 2011) among diabetic patients using MOP. Better adherence

among those using MOP has been demonstrated in other studies(Devine et al. 2010; Visaria 2012; Zhang et al. 2011), although one study(Khandelwal et al. 2011) had a null finding.

There are several possible explanations for these disparities in the effect of benefit changes. While one may expect greater price-sensitivity in vulnerable patients, the prepayment of the additional copayment required to receive the incentive was possibly more of a barrier for the vulnerable groups. The prepayment discount may have failed as an incentive if it was inadequately communicated to or understood by patients. We observed significantly lower uptake in those with inadequate health literacy, limited English proficiency, and among the two ethnic groups (Latinos and Asians) with the greatest number of non-English speaking patients compared to their respective reference groups (i.e., those with adequate health literacy and proficient in English, Caucasians). The reduced effect among patients with limited English proficiency is not unexpected. The health plan mailed a written notice of the benefit change (in English) to all the beneficiaries in advance of benefit design change, but did not distribute a Spanish-version of the notice until the year after the study. No other form of communication from the health plan was provided uniformly. We should expect that some patients would have additional information provided via discussion with the pharmacist when patients inquired about charges at the walk-in pharmacies. However, no subject-level data is available regarding those discussions.

The lower effect among those with inadequate health literacy may be attributable to difficulties navigating the complexities of the health system (i.e., understanding the steps needed to initiate a mail order refill); some patients may prefer the regular face-to-face interactions with pharmacists if they struggle with understanding written labels and medication instructions. Poor literacy is often accompanied by poor numeracy (i.e., the inability to understand and use numbers in daily life) which, though we did not asses this, may make it difficult for patients to weigh relative costs and benefits of the incentive. (Cavanaugh et al. 2008; Rothman et al. 2008) Lower income individuals may lack a credit card and be unaware that MOP can be requested via a mail-in form with a check, or be concerned about using a telephone or internet for credit card transactions. Some patients may be concerned about having medications sent to a mailbox that may be vulnerable to theft.

The benefit change offered a prepayment discount for MOP such that patients had a larger initial, out-of-pocket cost to obtain the discount (“pay to play” design), representing a larger burden for vulnerable patients with limited financial resources, a barrier compounded for patients taking multiple medications. After the benefit change, those receiving the less generous benefit had a substantial increase in cost-sharing (e.g., $21.33 per refill paid by those receiving the new benefit vs. $8.78 in the reference group). Thus, the prepayment burden was increased by the greater cost-sharing. More price sensitive patients may simply have had insufficient discretionary money or liquidity and were limited by the two copayments needed to benefit discount offer, or simply preferred “money in hand” over future savings provided by the incentive.

While the majority of subjects were dispensed 3 month supplies at each fill before and after the roll-out of the benefit change, the change to a less generous cost sharing arrangement

also resulted in a slight decrease (2.4 percentage points) in the proportion dispensed 3 month supply at each fill (from 85.5% before the benefit change to 83.1% after the benefit change) among those exposed to the benefit change. Our sensitivity analysis suggests there was an incentive effect in members who were dispensed 3 month supply before and after the benefit roll-out. Among the remaining minority of subjects who filled less than a 3 month supply during pre- and post-periods, we detected no significant incentive effect; there was no significant difference in MOP uptake among those who did vs. did not receive the benefit change. This sensitivity analysis suggests that the offered incentive will likely not stimulate MOP uptake among patients whose usual level of dispensing is less than a 3 month supply. It is important to note that 80% to 90% of health plan members fill a 3 month supply at each dispensing and stand to benefit from the incentive.

Some limitations and strengths should be noted. This is a study of a non-randomized exposure (benefit changes), and although we used a rigorous causal modeling approach (DID framework with marginal structural models) to handle biases associated with observational studies, residual confounding by measured or unmeasured variables are still a threat to validity. To isolate the effect of the benefit change on MOP from expected secular changes in MOP, we netted out the MOP uptake among those who had no change in benefits (i.e., the reference group). A limitation of this analytic approach is that there is no way to prove the validity of the DID assumption that the MOP uptake in the reference group serves as a reasonable model for the unobservable “background rates” of MOP uptake in the exposed group if they were actually not exposed. Thus we exercise caution when interpreting the quantitative findings. Because we studied a cohort of non-users, there were no prior trends in uptake to guide our predictions of future changes in utilization. However, given the magnitude of the quantitative differences in MOP uptake (i.e., >3-fold greater MOP uptake in 2006 among those exposed to the new benefit vs. those not exposed) and the substantially smaller benefit-related uptake in socially vulnerable populations, we believe that the qualitative interpretation of our findings regarding the uptake that is above and beyond background is reasonable; the benefit change with a prepayment discount for MOP stimulated MOP uptake, but less so in vulnerable populations. The stark differences in MOP uptake in patients receiving the pharmacy benefit change (vs. not) will likely diminish over time with growing acceptance for this new mode of medication delivery and as the number of remaining non-users decreases. Because this is observational research, interpreting the social differences in the impact of the benefit change is complicated given the exposed and reference groups differed on baseline social characteristics, although the final models adjusted for observed confounders. The ideal reference group would have been patients who were switched to a pharmacy benefit offering a 1 month supply (rather than remaining on the 3 month supply plan) without MOP incentives. No such benefit structure existed. Concerns of endogeniety arise if subjects can choose which level of benefits they were exposed to. However, during the time of this study, while the generosity of benefit coverage varied across employer group or Medicare, patients receiving benefits through any one of these contractors did not have a choice of level of benefit plan. All but 3% (n=351) of our study subjects acquired health plan coverage via employment or Medicare and thus had no choice about the level of coverage. The adjusted model accounts for differences in the

generosity of benefits by weighting for pharmacy benefit deductibles and pharmacy benefit business line.

To simply report the MOP uptake in those experiencing the benefit change would overestimate the effect of the benefit change given the secular trends. We reduced that MOP uptake resulting from the benefit change by the background expected uptake observed in the reference group, after adjusting for case mix differences. That said, the variation in uptake among from different social groups receiving the benefit change (i.e., exposed) conveys the same take home message; vulnerable subjects receiving the incentive were less likely to initiate MOP. For example, among those who did not use MOP prior to the benefit change, 44% of Caucasians vs. 21% of Latino and African Americans initiated MOP after receiving the benefit change. Although some of this MOP uptake would be expected due to secular trends and thus not due to the benefit change, the differential between social groups is consistent with a benefit change effect that differs is size across social strata.

The pharmacy benefit change combined the offer of a financial incentive, in the form of a prepayment discount, with a less generous pharmacy benefit plan. Those exposed to the benefit change were switched from a more generous baseline benefit to a much less generous benefit, and that may have impacted the magnitude of the incentive effect on MOP uptake. The financial incentive is the most plausible explanation for the increased MOP uptake. There is no obvious reason why charging patients more per pill (due to the increased cost sharing imposed by the benefit change) would induce the large increase in use of MOP that we observed overall or induce vulnerable patients to be less likely to take advantage of the MOP incentive that reduces the cost per pill. On the contrary, to the extent that vulnerable populations are more price-sensitive, they might be expected to be more likely to take advantage of the discount. Admittedly, we have no data available to explain why subjects made their choices regarding whether or not to initiate MOP. Substantive changes in adherence could change the motivation to use MOP or sample composition. One of the strengths of this study is that it was a natural experiment; the benefit change was not subject to patient choice or self-selection, but was dependent on group contract negotiations. Reverse causality is precluded also by the design's temporal ordering (i.e., pretest-posttest with controls) and regression to the mean is not a concern given both exposed and reference group have the identical starting point (none are MOP users at baseline).

This study suggests some policy-related lessons. Benefit change announcements using plain-language in English and other languages should be sent out prior to initiating the change. When both modes of medication delivery are supported by a health delivery system, pharmacists and pharmacy staff could verbally encourage the use of MOP and explain any potential cost savings associated with the MOP to patients currently using community pharmacies. Rather than requiring prepayment of an extra copayment to receive the discount, a more uniform effect may be achievable by restructuring the discount so that patients using MOP receive a set number of free days' supply for each copayment. "Pay to play" designs such as this may in the end act as a disincentive that overrides the benefit of any potential discounts for the patient in a way that differentially impacts vulnerable populations. While largely dictated by external forces (e.g., competitive health plan markets, group purchaser and federal insurer demands, rising cost of pharmaceuticals and provision

of health care), benefit changes present a difficult policy dilemma for healthcare delivery systems given the often competing economic and quality implications. In this case, the health plan benefit change simultaneously supported one quality improvement goals (e.g., increase use of MOP) and potentially reduced the cost of pharmacy operations, while competing with another (e.g., elimination of health disparities). These findings further demonstrate the hazard of assuming uniform effects of innovations, interventions or structural changes across patient groups. While we expect that inequalities in use of MOP will shrink as advantaged groups approach a ceiling and the disadvantaged groups catch up, the pattern needs to be viewed in the larger context. Even if the inequalities resulting from any given structural change eventually dissipate, the constant stream of new structural changes can perpetuate or exacerbate existing inequalities if even small and temporary differences in health system access are progressively introduced (see Phelan and Link's theory of “fundamental causes”(Phelan and Link 2005; Phelan et al. 2004)). To avoid increasing existing social differences in utilization, early testing for heterogeneity in treatment effectiveness provides an important opportunity to proactively design and tailor innovations, whether they be new benefit models, translation of interventions, or quality improvement efforts.(Frohlich and Potvin 2008; Varadhan et al. 2012)

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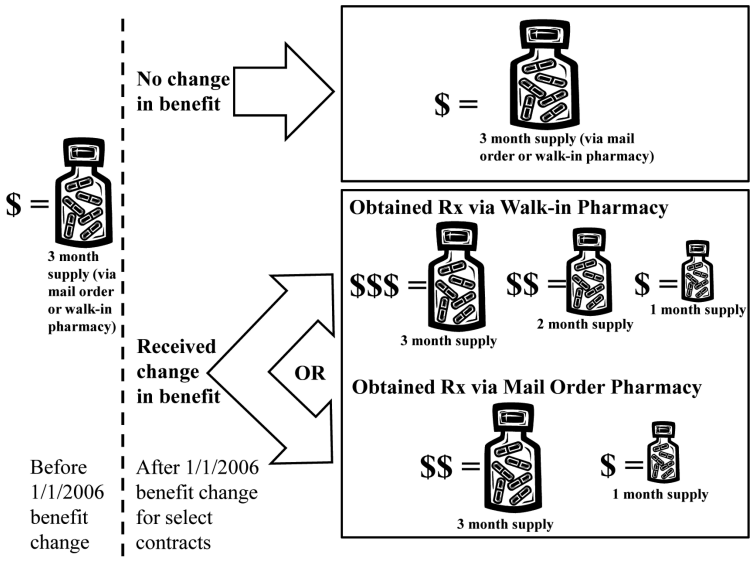

*Note: $=1 copayment; $$=2 copayments; $$$=3 copayments.

Figure 1.

Impact of the January 1, 2006 benefit change for select patients on their cost sharing and duration of supply dispensed for patients obtaining their medications via walk-in vs. mail order pharmacy. Note that the copayment* per dispensing varies (typically from $5 to $15 per copayment) and depends on the individual's contract.

Table 1

Characteristics (unadjusted*) of the 10,590 KPNC patients who had not used mail order pharmacy prior to baseline date of pharmacy benefit change (1/1/2006)

Patient characteristics	All (n=10,590)	Pharmacy benefit change in 2006		
		Yes (n=2,442)	No (n=8,148)	p-value for unadjusted difference†
Demographics				
Female	5,332 (50.4)	1,309 (53.6)	4,023 (49.4)	0.0002
Mean age (in years) (SD)	59.7 (10.1)	64.8 (10.1)	58.2 (9.6)	< 0.0001
Race/ethnicity				<0.0001
African American	2,126 (20.1)	345 (14.1)	1,781 (21.9)	
Asian	1,101 (10.4)	284 (11.6)	817 (10.0)	
Caucasian	1,955 (18.5)	546 (22.4)	1,409 (17.3)	
Filipino	1,398 (13.2)	232 (9.5)	1,166 (14.3)	
Latino	2,053 (19.4)	618 (25.3)	1,435 (17.6)	
Multi-racial	1,164 (11.0)	251 (10.3)	913 (11.2)	
Other/unknown	793 (7.5)	166 (6.8)	627 (7.7)	
Education				< 0.0001
No degree	1,839 (17.8)	694 (29.5)	1,145 (14.3)	
High school/GED	3,086 (30.0)	730 (31.0)	2,365 (29.5)	
Some college	2,613 (25.3)	503 (21.4)	2,110 (26.4)	
College graduate	2,808 (27.1)	427 (18.1)	2,381 (29.8)	
Annual Income (in thousands)				< 0.0001
<$25K	1,891 (21.4)	906 (45.6)	985 (14.4)	
$25K-$49K	2,709 (30.6)	584 (29.4)	2,125 (31.0)	
$50K-$79K	2,176 (24.6)	278 (14.0)	1,898 (27.7)	
≥$80K	2,074 (23.4)	219 (11.0)	1,855 (27.0)	
Reported difficulties paying for medications	661 (7.9)	262 (14.0)	399 (6.2)	< 0.0001
Reported difficulties paying for food	2,603 (26.7)	732 (32.8)	1,871 (24.8)	< 0.0001
Reported difficulties paying for medical supplies	403 (5.7)	142 (9.2)	261 (4.8)	< 0.0001
Any financial hardship (for food, Rx, or med supplies)	2,969 (38.4)	875 (49.1)	2,094 (35.2)	< 0.0001
Limited English Proficiency	1,086 (12.3)	394 (19.8)	692 (10.1)	< 0.0001
Inadequate health literacy	3,297 (46.3)	909 (57.7)	2,388 (43.1)	< 0.0001
Mean home to local pharmacy distance in miles (SD)	6.5 (9.2)	7.0 (10.7)	6.4 (8.8)	0.005

*n (%) unless otherwise specified; Column percentages shown

†p-value for Chi-square test for categorical variables and t-test for continuous variables

Table 2

Out of pocket costs and utilization before and after pharmacy benefit change 10,590 KPNC patients who had not used mail order pharmacy prior to baseline date of pharmacy benefit change (1/1/2006)

Patient characteristics	All (n=10,590)	Pharmacy benefit change (before weighting)		
		Yes (n=2,442)	No (n=8,148)	p-value for unadjusted difference[§]
12 months prior to baseline[†]				
Per day per medication cost[‡], for community pharmacy fills, mean (SD)	$0.17 ($0.38)	$0.23 (0.36)	$0.15 ($0.38)	< 0.0001
Total incurred cost per refill, for community fills, mean (SD)	$9.62 ($8.53)	$13.65 ($13.04)	$8.42 ($6.11)	< 0.0001
Days' supply dispensed, for community fills, mean (SD))	89 (16)	87 (18)	89 (15)	< 0.0001
1 month supply dispensed	784 (7.4)	251 (10.3)	533 (6.5)	< 0.0001
2 months supply dispensed	347 (3.3)	69 (2.8)	278 (3.4)	0.15
3 months supply dispensed	9,293 (87.8)	2,087 (85.5)	7,206 (88.4)	< 0.0001
Total dispensings, for community fills, mean (SD)	14.3 (7.8)	15.0 (7.8)	14.1 (7.8)	< 0.0001
Cost-sharing 12 months after baseline[†]				
Per day per medication cost[‡], for community pharmacy fills, mean (SD)	$0.20 ($0.39)	$0.35 ($0.48)	$0.16 ($0.35)	< 0.0001
Per day per medication cost[‡], for mail order pharmacy fills, mean (SD)	$0.18 ($0.22)	$0.28 ($0.26)	$0.09 ($0.12)	< 0.0001
Total incurred cost per refill, for community fills, mean (SD)	$11.64 ($10.62)	$21.33 ($15.27)	$8.78 ($6.21)	< 0.0001
Total incurred cost per refill, for mail order pharmacy fills, mean (SD)	$15.97 ($16.93)	$24.23 ($18.26)	$7.77 ($10.27)	< 0.0001
Days supply dispensed, for:				
Community pharmacy fills, mean (SD)	88 (16)	83 (20)	90 (15)	< 0.0001
Mail order pharmacy fills, mean (SD)	91 (18)	95 (13)	87 (22)	< 0.0001
1 month supply dispensed	801 (7.6)	336 (13.8)	465 (5.7)	< 0.0001
2 months supply dispensed	246 (2.3)	48 (2.0)	198 (2.4)	0.18
3 months supply dispensed	9,417 (88.9)	2,030 (83.1)	7,387 (90.7)	< 0.0001
Total dispensings, for:				
Community pharmacy fills, mean (SD)	14.7 (8.1)	14.0 (8.8)	14.9 (7.9)	< 0.0001
Mail order pharmacy fills, mean (SD)	5.6 (5.5)	8.0 (6.3)	3.2 (3.3)	< 0.0001
Insurance Type				
Part D group coverage (%)	1,454 (13.7)	22 (0.9)	1,432 (17.6)	< 0.0001
Part D individual coverage (%)	1,814 (17.1)	1,817 (74.3)	0	
Non-Medicare coverage (%)	7,322 (69.1)	606 (24.8)	6,716 (82.4)	

*n (%) unless otherwise specified; Column percentages shown

[†]2005 vs 2006 used for pre-post comparison of those not receiving the benefit

[‡]Per day medication cost equals the patient out-of-pocket cost divided by the days supply dispensed.

[§]p-value for Chi-square test for categorical variables and t-test for continuous variables

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Table 3

Uptake of Mail Order Pharmacy Use (MOP) following baseline date of pharmacy benefit change, benefit change effect, and effect difference (difference in benefit change effect across social groups) in a cohort of 10,590 diabetes patients.

	MOP uptake		Benefit change effect*		Effect Difference§ (95% CI)
	Pharmacy benefit changed	No benefit change	Unadjusted (95% CI)	Adjusted‡ (95% CI)	
All subjects	0.30	0.09	0.21 (0.19, 0.23)	0.26 (0.22,0.30)	----
Income					
<$25K (ref)	0.25	0.08	0.18 (0.14, 0.21)	0.26 (0.19, 0.32)	---
$25K-$49K	0.32	0.08	0.24 (0.20, 0.28)†	0.21 (0.14, 0.29)	−0.05 (−0.15, 0.05)
$50K-$79K	0.34	0.08	0.25 (0.20, 0.31)†	0.34 (0.23, 0.46)	0.08 (−0.05, 0.22)
$80K +	0.37	0.12	0.26 (0.19, 0.32)†	0.27 (0.14, 0.40)	0.02 (−0.13, 0.16)
Race					
Caucasian(ref)	0.44	0.12	0.32 (0.28, 0.37)	0.37 (0.31, 0.44)	---
African Am.	0.21	0.08	0.13 (0.09, 0.18)†	0.25 (0.14, 0.38)	−0.12 (−0.25, 0.04)
Asian	0.39	0.11	0.28 (0.22, 0.34)	0.21 (0.10, 0.34)†	−0.16 (−0.30, −0.001)†
Filipino	0.25	0.08	0.17 (0.11, 0.23)†	0.22 (0.10, 0.37)	−0.15 (−0.29, 0.02)
Latino	0.21	0.06	0.15 (0.12, 0.19)†	0.14 (0.07, 0.20)†	−0.24 (−0.33, −0.14)†
Education					
No degree (ref)	0.25	0.07	0.18 (0.14, 0.22)	0.22 (0.15, 0.30)	---
HS/GED	0.29	0.09	0.20 (0.16, 0.24)	0.26 (0.19, 0.33)	0.04 (−0.07, 0.14)
Some college	0.33	0.09	0.25 (0.20, 0.29)†	0.23 (0.16, 0.32)	0.01 (−0.10, 0.13)
College +	0.38	0.10	0.29 (0.24, 0.34)†	0.31 (0.21, 0.41)	0.09 (−0.05, 0.21)
Limited English Proficiency					
No (ref)	0.33	0.09	0.24 (0.21, 0.27)	0.27 (0.23, 0.32)	---
Yes	0.21	0.06	0.15 (0.10, 0.20)†	0.13 (0.06, 0.21)†	−0.14 (−0.22, −0.05)†
Inadequate Health Literacy					

	MOP uptake		Benefit change effect*		Effect Difference§ (95% CI)
	Pharmacy benefit changed	No benefit change	Unadjusted (95% CI)	Adjusted‡ (95% CI)	
No (ref)	0.40	0.09	0.31 (0.27, 0.35)	0.35 (0.27, 0.42)	----
Yes	0.26	0.08	0.18 (0.15, 0.21)†	0.20 (0.14, 0.26)†	−0.15 (−0.24, −0.05)†
Financial hardship					
No (ref)	0.36	0.09	0.27 (0.23, 0.30)	0.31 (0.24, 0.37)	---
Yes	0.26	0.09	0.19 (0.16, 0.22)†	0.24 (0.17, 0.31)	−0.07 (−0.16, 0.02)

*Benefit change effect is estimated by the MOP uptake among those with a benefit change after subtracting the uptake in those without a benefit change (to "net out" the MOP uptake due to secular time trends among those not affected by the benefit change). All risk differences in table were significant at the <0.05 level for H_0: RD=0;

†Indicates statistical significance at the ≤ 0.05 level for H_0: $RD_{(level)} = RD_{(reference)}$

‡Poisson model with identity link function, models weighted for inverse probability of treatment weights (IPTW), expansion weights for race-stratified sampling design, and survey non-response (Horvitz-Thompson weighting). The IPTW model included baseline age, out of pocket drug copay, benefits based copay for brand drugs, Medicare indicator, deductible drug plan indicator, drug benefit business line (e.g., large employer group, small employer group, strategic group) and our socioeconomic indicators (ethnicity, income, education, limited English proficiency, inadequate health literacy or financial hardship); weights were truncated at the 99^{th} percentile. Confidence intervals calculated using 1,000 bootstrap samples in the adjusted models.

§Effect Difference is the absolute difference in the adjusted benefit change effect between a given social strata and the reference social strata